THE CORRELATION OF TRANSAMINASES AND LIVER DISEASES

Bastianus Alfian Juatmadja, I Wayan Putu Sutirta Yasa, DAP Rasmika Dewi, Bagus Komang Satriyasa
Department of Clinical Pathology Faculty of Medicine Udayana University / Sanglah Hospital

ABSTRACT

The symptoms of liver diseases are very diverging, from the mild one till the severe one. Sometimes we may find that severe heart disorders but the symptoms are too less. We need some tools to make a good diagnosis. We can not only use a good anamnesis, but also have to use good physical examination and the other support test. Transaminase also called aminotransferase. This aminotransferase catalyzes the transfer of the amino group (−NH2) of an amino acid to a carbonyl compound. The liver contains specific transaminases for the transfer of an amino group from glutamic acid to α-keto acids that correspond to most of the other amino acids. Other transaminases catalyze reactions in which an amino group is transferred from glutamic acid to other compounds. Transamination is one of the principal mechanisms for the formation of necessary amino acids in the metabolism of proteins. Transaminase as a sign to cell damage may divided into Serum Glutamic Oxalocetic Transaminase **(**SGOT), Serum Glutamic Pyruvic Transaminase (SGPT), and Lactic Dehydrogenase (LDH). Gamma GT and alkali fosfatase correlate with cholestasis. Cholinestrase correlate with liver synthesis capacity.

Keywords: Transaminase, amino group, α-keto acids

Introduction

Early detection to these liver diseases is absolutely needed to decrease the morbidity and mortality. Early detection means early treatment. A good and precise treatment may decrease the diseases progressivity and may cure the diseases[1].

Among the most sensitive and widely used blood tests for evaluating patients with hepatitis are the liver enzymes, called aminotransferases. They include aspartate aminotransferase (AST or SGOT) and alanine aminotransferase (ALT or SGPT). These enzymes normally are contained within liver cells. If the liver is injured (as in viral

hepatitis), the liver cells spill the enzymes into the blood, raising the enzyme levels in the blood and signaling that the liver is damaged[1].

The most useful aminotransferase are SGPT, gamma GT and CHE. SGPT is used to find the cell damage, gamma GT is used as a sign of cholestasis and CHE is used as a sign of liver synthesis disorder[1].

The Abnormalities of ALT

Alanine transaminase (ALT) is an enzyme found in the highest amounts in the liver. Injury to the liver results in release of the substance into the blood. The normal range of values for ALT is from 7 to 56 units per liter of serum. An increase in ALT levels may be due to Acute pancreatitis, Celiac disease, Cirrhosis, Death of liver tissue (liver necrosis), Hepatitis (viral, autoimmune), Hereditary hemochromatosis , Infectious mononucleosis, Lack of blood flow to the liver (liver ischemia), Liver disease, Liver tumor, Use of drugs that are poisonous to the liver[2].

The Abnormalities of AST

AST (aspartate aminotransferase) is an enzyme found in high amounts in heart

muscle and liver and skeletal muscle cells. It is also found in lesser amounts in other tissues. The normal range of values for AST is from 5 to 40 units per liter of serum. An increase in AST levels may indicate acute hemolytic anemia, acute pancreatitis, acute renal failure, Cirrhosis, heart attack, hepatitis, hereditary hemochromatosis,infectious mononucleosis, lack of blood flow to the liver (liver ischemia), liver necrosis, Liver tumor, multiple trauma,

primary muscle disease, progressive muscular dystrophy, recent cardiac catheterization or angioplasty, recent convulsion, recent surgery, severe deep burn, skeletal muscle trauma, use of drugs that are poisonous to the liver[3].

The Abnormalities of Cholinesterase

Serum cholinesterase is a test that looks at blood levels of certain enzymes (acetylcholinesterase and pseudocholinesterase) that help the nervous system work properly. Acetylcholinesterase (also known as RBC cholinesterase) and pseudocholinesterase (also known as butyrylcholinesterase or plasma cholinesterase) help break down a chemical that nerves need to send signals. Decreased pseudocholinesterase levels may be due to acute infection, chronic malnutrition, heart attack, liver damage, metastasis, obstructive jaundice, poisoning from organophosphates (chemicals found in some pesticides), and smaller decreases may be due to pregnancy, use of birth control pills. Acetylcholinesterase is found in nerve tissue and red blood cells. Pseudocholinesterase is found primarily in the liver[3].

The Abnormalities of LDH

Lactate dehydrogenase (LDH) is found in many body tissues like the heart, liver, kidney, skeletal muscle, brain, blood cells, and lungs. LDH exists in 5 forms, which differ slightly in structure. LDH-1 is found primarily in heart muscle and red blood cells. LDH-2 is concentrated in white blood cells. LDH-3 is highest in the lung. LDH-4 is highest in the kidney, placenta, and pancreas. LDH-5 is highest in the liver and skeletal muscle. All of these can be measured in the blood[4].

Normally, the level of LDH-2 is greater than LDH-1. Greater-than-normal LDH levels may suggest heart attack, hemolytic anemia, hypotension, infectious mononucleosis, intestinal ischemia (blood deficiency) and infarction (tissue death), liver disease such as hepatitis, muscle injury, muscular dystrophy, pancreatitis, lung tissue death, stroke, and ischemic cardiomyopathy[4].

The Abnormalities of GGT

The normal of gamma-glutamyl transpeptidase (GGT) range is 0 to 51 international units per liter (IU/L) but normal value ranges may vary slightly among different laboratories. Greater-than-normal levels of GGT may indicate congestive heart failure, cholestasis (congestion of the bile ducts), cirrhosis, hepatitis, liver ischemia (blood flow deficiency), liver necrosis, liver tumor, use of hepatotoxic drugs (drugs toxic to liver)[2].

Possible Diseases that Signed by The Increasing of Transaminases

Elevated blood levels of AST and ALT only means that the liver is inflamed, and elevations can be caused by many agents other than hepatitis viruses, such as medications, alcohol, bacteria, fungus, etc. In order to prove that a hepatitis virus is responsible for the elevations, blood must be tested for antibodies to each of the hepatitis viruses as well as for their genetic material[2].

We may use few classifications to simplify the understanding about these transaminases and liver diseases. These classifications are transaminases disorders in (1) acute viral hepatitis, (2) liver toxicity, (3) chronic hepatitis, (4) bile duct disease and cirrhosis bilier, (5) fatty liver, and (6) liver tumor[1].

Acute Viral Hepatitis

Acute viral hepatitis may caused by hepatitis virus A, B, C, D, E, mononukleosis virus, yellow fever, cytomegalovirus, and dengue[1].

Typical symptoms of acute hepatitis are fatigue, anorexia, nausea, and vomiting. Severe cases of acute hepatitis may progress rapidly to acute liver failure, marked by poor hepatic synthetic function[5].

Patients with acute viral hepatitis (for example, due to hepatitis A or hepatitis B) can develop very high AST and ALT levels (sometimes in the thousands of units per liter range). These high AST and ALT levels will become normal in several weeks or months as the patients recover completely from their acute[6].

Acute hepatitis without complications, the degree of the cell damage is light but the cell inflamation is severe. In acute hepatitis, transaminase may rise into 2,000 unit / liter, while alkali phosphatase and gamma GT raise slightly only. Gamma GT concentration is usually less than SGOT concentration. Cholinestrase will decrease slightly on second week and then increase on fourth week in convalescent period. De ritis ratio between SGOT and SGPT is less than 1[1].

While monitoring every two weeks till four weeks, gamma GT and SGPT are the last number to be normal. In case, the decreasing of SGOT and SGPT are not done in six till twelve weeks, the diagnosis of chronic hepatitis may be suspected[1].

Liver Toxicity

Drugs and foods may have toxicity effect to the liver. Halotan may caused liver damage, which the signs are increasing of SGOT, while gamma GT and ALP in normal concentration. The damage which caused by this halotan is liver necrosis central. Drugs that suppress the thyroid such as metimazole will obstruct the biliary tract and give the signs of increasing gamma GT and ALP. Liver damage that caused by contraceptive drugs shows increasing of SGOT, SGPT concentrations and decreasing of alkali phosphatase, cholinestrase concentrations also normal or increasing slightly of gamma GT and ALP concentrations. Slight increasing of SGOT and SGPT usually as a sign of hepatitis that caused by the drugs[1].

Chronic Hepatitis

Chronic hepatitis classified into: (1) persistent chronic hepatitis, (2) active chronic hepatitis, and (3) hepatic cirrhosis[1].

Persistent chronic hepatitis may show slight increasing of SGOT and SGPT. SGOT and SGPT usually increase 2 – 3 times from the normal concentration value and gamma GT usually less than SGOT. Alkali phosphatase, CHE, and coagulant enzyme in normal concentration value[1].

The hepatocellular damage in active chronic hepatitis is more severe. SGOT and SGPT usually increase 5 or 10 times from the normal concentration value. Gamma GT usually less than SGOT[1].

Abnormal elevation of liver enzymes in the blood suggests inflammation or injury to the liver from many causes as well as cirrhosis[7]. De ritis ratio between SGOT and SGPT usually more than one. Cholinestrase coagulant enzyme will decrease in severe liver damage[1].

Aminotransferase levels can be normal during chronic hepatitis if the disease is quiescent, particularly with HCV. Alkaline phosphatase is usually normal or only slightly elevated but is occasionally markedly high[8].

Bile Duct Disease and Cirrhosis Biliary

The increasing of alkali phosphatase and gamma GT are clearly seen in biliary tract disorder. The increasing of SGOT and SGPT also may occur in acute obstruction of biliary tract or chronic obstruction that have damaged the liver parenchyma. In contrast, the increasing of SGOT and SGPT not occurred in cholelithiasis[1].

Cholangitis will be signed by the increasing of body temperature, ALP, LAP, and gamma GT. We also find the increasing of ALP, LAP, and gamma GT in biliary cirrhosis. Cholinestrase and coagulant enzyme will decrease in progressive liver disease[1].

Fatty Liver

We may find the increasing of transaminase 2 – 3 times from the normal concentration value. There are alcoholic fatty liver disease which caused by alcohol. It will progress to alcoholic steatohepatitis. Non-alcoholic fatty liver disease (NAFLD) may progress to non-alcoholic steatohepatitis (NASH) which caused is usually idiopathic.

Alcoholic fatty liver disease may show Elevations of aminotransferases are moderate (< 300 IU/L) and do not reflect the extent of liver damage. The ratio of AST to ALT is ≥ 2. The basis for low ALT is a dietary deficiency of pyridoxal phosphate (vitamin B6), which is needed for ALT to function. Its effect on AST is less pronounced. Serum γ–glutamyl transpeptidase (Gamma GT) increases caused by ethanol induces this enzyme. Serum albumin may be low, usually reflecting undernutrition but occasionally reflecting otherwise obvious liver failure with deficient synthesis[9].

The most frequent biochemical abnormality in the blood in NASH is persistent, mild to moderately elevated transaminases (ALT and AST). In NASH, their levels tend to fluctuate from month to month, and most often the ALT is greater than the AST[10].

Liver Tumor

Liver tumor may shows the increasing of alkali phosphatase and gamma GT. SGOT and SGPT in normal concentration value when hepatocellular carcinoma in early stage but in the late stage while the cell damage more severe, SGOT and SGPT will increase[1].

An elevated perioperative ALT level($p = 0.021$), multiple tumor nodules in the resected specimen ($p < 0.001$), and a tumor size greater than 5 cm ($p = 0.001$) were significant independent risk factors for tumor recurrence. The latter two factors were also independent prognostic factors for overall survival and disease-free survival. An elevated ALT level was an independent prognostic factor for disease-free survival ($p = 0.025$)[11].

Summary

We need a good tool to do a screening test for liver diseases. If we could diagnose the liver disease as soon as possible, we may treat the disease appropriately. Finally it will decrease the morbidity and mortality. Not only decrease the morbidity and mortality but also we may increase the patients quality of life. Early detection with an appropriate treatment may decrease the cost also. In the other words, it has a financial benefit also.

We may use the transaminases to do a screening test. These transaminases are enzymes that located normally outside and inside the cells. If the cells are broken down, the transaminases will goes outside the cells which increase the concentration transaminases outside the cells that can be detected in the blood. Mostly, the increasing of these transaminases are earlier than the symptoms, so we may detect the diseases as soon as possible in early stage. This is the benefit of these transaminases.

Although, this transaminases pattern may help us to make a diagnosis for liver diseases, we may need the other exam to make an accurate diagnosis. Sometimes, even though we already done all transaminases exam, we cannot have a definite diagnosis. In this case, we have to do morphologic or histopatologic exam. This is the paucity of transaminases.

REFERENCES

1. Akbar N. Kelainan Enzim Pada Penyakit Hati. In: Sudoyo AW, Setiyohadi B, Alwi I, Simadhibarata MK, Setisti S (eds). 4th ed. Jakarta: PDSPDI; 2006. p. 426-8
2. Dugdale DC, Zieve D. ALT. MedlinePlus [cited 22nd February 2009]. Available from: http://www.nlm.nih.gov/medlineplus/ency/article/003473.htm
3. Dugdale DC, Zieve D. AST. MedlinePlus. [cited 23rd February 2009]. Available from: http://www.nlm.nih.gov/medlineplus/ency/article/003472.htm
4. Vorvick L, Zieve D. LDH Isoenzymes. MedlinePlus. [cited 14th March 2009]. Available from: http://www.nlm.nih.gov/medlineplus/ency/article/003499.htm
5. Wolf, DC. Emedicine. Liver: Hepatitis Viral. [cited 1st July, 2009]. Available from: http://emedicine.medscape.com/article/185463-overview
6. Lee D, Marks JW. Digestion center: Viral Hepatitis. medicinenet [cited 7th January 2010]. Available from: http://www.medicinenet.com/viral_hepatitis/page4.htm#5howis
7. Lee D, Marks JW. Digestion center: Cirrhosis. medicinenet [cited 7th January 2010]. Available from: http://www.medicinenet.com/cirrhosis/page4.htm#tocg
8. Cohen S. Hepatic and Biliary Disorders: Chronic hepatitis. Merck. [cited February 2007]. Available from: http://www.merck.com/mmpe/sec03/ch027/ch027c.html
9. Shaffer EA . Hepatic and Biliary Disorders: Alcoholic Liver Disease. Merck [cited June 2009]. Available from: http://www.merck.com/mmpe/sec03/ch025/ch025a.html
10. Mendler M, Schoenfield LJ. Digestion center: Fatty liver. medicinenet [cited 7th January 2010]. Available from: http://www.medicinenet.com/fatty_liver/page9.htm#tocp

11. Cheung YS, Chan HLY, Wong J, Lee KF, Poon TCW, Wong N, Lai PBS. Elevated Perioperative Transaminase Level Predicts Intrahepatic Recurrence in Hepatitis B-related Hepatocellular Carcinoma After Curative Hepatectomy. Asian Journal of Surgery.2008; 31(2): 41-9